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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,363	11/15/2001	Richard C. Duke	3923-3	2524

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,363	DUKE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,29 and 31-33* is/are pending in the application.

4a) Of the above claim(s) *4-7,10 and 16-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8, 9, 11-15, and 29, and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

5.0.0

DETAILED ACTION

1. Currently, claims 1-25, 29, and 31-33 are pending in the application. In the prior action, mailed on September 9, 2004, claims 1-25 and 29-33 were pending; with claims 1-3, 8, 9, 11-15, and 29-33 rejected, and claims 4-7, 10, and 16-25 withdrawn as to non-elected inventions. In the Response, filed on March 8, 2005, the Applicant amended claims 1-16, 23-25, 29, and 31-33; and cancelled claim 30.

2. Currently, claims 1-3, 8, 9, 11-15, 29, and 31-33 are under consideration.

3. Because this action raises new grounds of rejection (restatement of the obviousness rejection over Paglia, Barbera-Guillemm, and Duke), it is made Non-Final.

Priority

4. **(Prior Objection- Withdrawn)** In the prior action, it was noted that application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). In view of the amendment properly making this reference, and in view of the recognition of the claim to priority in the Filing Receipt mailed on March 20, 2002 (copy attached) the objection to the claim of priority is withdrawn. Applicant's claim to priority is acknowledged.

Applicant's submission of a copy of the filing receipt as requested by telephone by the Examiner on June 8, 2005 is appreciated.

Claim Rejections - 35 USC § 101

5. **(Prior Rejection- Withdrawn)** Claims 1-3, 8, 9, 11-15, and 29-33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In view of the amendment of the claims to read on compositions comprising isolated dendritic cells, the rejection is withdrawn.

Claim Objections

6. **(New Objection- Necessitated by Amendment)** Claim 15 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the present case, claim 1 was amended to include the limitations of dependent claim 15. Thus, claim 15 no longer provides additional limitations over those presented in claim 1, and therefore reads on identical subject matter.

Claim Rejections - 35 USC § 112

7. **(Prior Rejection- Withdrawn)** Claims 1, 2, 3, 8, 9, 11-15 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions wherein the dendritic cells are loaded with either whole cell or spheroplast yeast vehicles and an antigen, does not reasonably provide enablement for therapeutic compositions wherein the dendritic cells is loaded with any yeast vehicle and an antigen. The claims were rejected on two grounds.

First, the claims were rejected as not enabled for the full scope of the yeast vehicles described in the claims. In view of the Applicant's amendment of the claims limiting them to the use of specified types of yeast vehicles, and the Applicant's arguments with respect to the definition of "a subcellular yeast particle," the rejection is withdrawn on this basis.

The second ground of rejection was that the Applicant had not provided an enabling description of the claimed inventions to the extent that they read on "therapeutic" compositions to any antigen or disease. In the Response, the claims were amended to read on "immunogenic" compositions rather than on "therapeutic" compositions. In view of this, the second basis of this rejection is withdrawn.

Claim Rejections - 35 USC § 103

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. **(Prior Rejection- Maintained and Restated)** Claims 1-3, 8, 9, and 29-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Barbera-Guillem (U.S. Pub 2002/0155108) and Paglia et al. (J Exp Med, 183: 317-22) in view of Duke et al. (U.S. Patent 5,830,463). These claims read on therapeutic compositions comprising a dendritic cell (DC), a yeast vehicle, and at least one antigen. It is noted that claims 11-15 were not previously rejected based on this combination. However, as the Duke reference teaches the limitations of these claims (see e.g., column 7 lines 25-34, column 12 lines 36-39, and column 6 lines 14-60), these

claims are hereby added to the rejection. Claim 30 has been cancelled from the application. The rejection is therefore withdrawn from this claim. Claims 1-3, 8, 9, 11-15, 29, and 31-33 stand rejected.

The Applicant traverses this rejection by asserting that there is no motivation to combine the references, and that the presently claimed invention demonstrates unexpected results over the prior art. In support of the assertion that there is no motivation to combine the references, the Applicant submits two arguments. First, the Applicant argues that there is no motivation to combine the teachings of Duke with the other references because there is no motivation in the references to use the yeast vehicles of Duke to administer antigens to the dendritic cells of the other references ex vivo. Second, the Applicant argues that even if there was motivation to combine the method of Duke with that of the other references. With respect to the unexpected results assertion, the Applicant argues that the present invention achieves improves results without the need for a booster as is required for the use of DCs with antigen alone. These arguments are not found persuasive.

Suggestion and motivation to combine

The Applicant's first two arguments in traversal are directed to the motivation to combine. First, the Applicant asserts that there is "no suggestion, motivation or expectation of success at making and using the present invention found in the combination of Duke with either of Barbera-Guillem or Paglia et al." In support of this argument, the Applicant contends that Duke does not teach the provision of a therapeutic composition comprising isolated dendritic cells (DCs) that have been loaded intracellularly with a yeast vehicle and an antigen.

The phase "intracellularly loaded" is described in the present application to include any means of getting the yeast vehicle and the antigen into a cell. Page 16. The application indicates that such means may include the forcing of the vehicle into the cells, or placing the vehicles "in an environment (e.g. in contact with or neat to a cell) where the [vehicle] will be substantially likely to enter the cell by some process (e.g. phagocytosis)." Page 16, lines 20-23. As indicated in the prior action, the Duke reference teaches that the yeast vehicles disclosed therein may be used to contact a population of cells under conditions where the vehicle is adsorbed by the targeted cells. Column 19, lines 18-34. The reference teaches that such cells may be administered to an animal for the induction of an immune response. Id. Thus, the reference teaches compositions wherein the yeast vehicle has been intracellularly loaded, and the administration of the cells to an animal for the induction of an immune response. The Applicant's first argument, that there is no suggestion for the intracellular loading of the yeast vehicles into cells is therefore not found persuasive.

The Applicant's second argument against motivation to combine is that there is not motivation for the combination of the method of Duke with the loading methods of the other two references. The Applicant argues that neither of the Paglia and Barbera-Guillem references provides a motivation to combine their teachings with those of Duke. However, the Duke reference provide such a motivation in its teachings that the use of the yeast vehicles not only permits the activation of both humoral and cellular immune reactions, but that the use of these vehicles avoids the need for additional adjuvants, and does not cause side affects that may be found with the use of other adjuvants. See e.g., column 5 lines 10-44. Thus, motivation to combine may be found in the Duke reference.

The Applicant's arguments that the Paglia and Barbera-Guillem references fail to teach that a different mode of antigen delivery is required have been considered. However, these references do not teach away from the present combination. Rather, they provide teachings only as to the best mode of antigen delivery known to the authors of those references. They provide no basis on which those in the art would later determine that another mode of delivery, disclosed as superior is certain respects, would not operate in the delivery of antigens to the dendritic cells. Because the teachings of Duke provide motivation to use the yeast vehicles disclosed therein as the means for the delivery of the antigens, the teachings of this reference are sufficient to combine the teachings of the references. With respect to the assertion that there is no motivation to use both the method of either Paglia or of Barbera-Guillem, it is noted that the rejection is on the basis of the use the method of Duke for the loading of cells as an alternative to the methods of the other references, and not the use of a combination.

The Applicant's arguments with respect to the lack of motivation to combine are therefore not found persuasive.

Unexpected results.

The Applicant's third argument in traversal is that the claimed inventions have unexpected results over either the DCs of Paglia and Barbera-Guillem, and the yeast cells of Duke. It is first noted that the asserted showings of unexpected results, are not commensurate in scope with the claims. Each of the examples cited by the Applicant relates to experiments only with recombinant live yeast. There is no demonstration that what unexpected results may be found would be common to each of the different yeast vehicles encompassed by the claims.

Second, with respect to the asserted unexpected results using the DCs pulsed with the live yeast vectors of Example 7 of the present application, it is noted that the improved results were only seen when the cells were administered by a particular (subcutaneous) route. It is not clear from the example whether the yeast vehicles (no DC) against which the subcutaneous administration is being compared were also administered subcutaneously. However, it is clear that the yeast vehicles injected into the mice of that example achieved better results than the intrperitonially administered compositions. It is therefore not clear if the claimed compositions are in fact achieving unexpected results over the prior art compositions.

Additionally, it is not clear that the improved results are unexpected. The teachings of the Duke reference indicate that it is not unexpected that the use of the yeast vehicles would achieve improved results over antigens alone. Based on these teachings, and the indication in the Duke reference that the yeast vehicles were able to induce immune responses in immune cells absent the use of adjuvants, it is not clear that those in the art would have found it surprising that the claimed DC cells would be more effective than those stimulated only with pulsed antigens.

Because it is not clear that the claimed compositions do in fact achieve unexpected results over the previously known compositions, or that what improved efficacy the compositions achieve would be unexpected in light of the teachings of the Duke reference, the Applicant's arguments with respect to unexpected results are not found persuasive. The rejection is therefore maintained for the reasons above and the reasons of record.

10. **(Prior Rejection- Maintained)** Claims 1-3, 8, 9, and 11-15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Duke in view of the teachings of

Tomai. The claims have been described above, and the teachings of the identified references were described in the prior action. In traversal of this rejection, the Applicant argues that Tomai provides no motivation for the combination of the teachings of these references. The Applicant argues that Tomai teaches a different means of inducing the immunogenicity of the DC cells from the methods of Duke, and that those in the art would have had no motivation to use the methods of Duke in combination with the use of the imidazoquinoline as taught by Tomai. The Applicant further argues that the claimed compositions have unexpected results over the combination suggested by the prior art. These arguments are not found persuasive.

As noted previously, the Tomai reference teaches the activation of DCs, and exposure thereof to antigens, to produce and immunogenic composition comprising the cells. The teachings of Duke also provide a method for the activation and introduction of antigens to cells. While Duke does not specifically teach the use of the yeast vehicles disclosed therein for the delivery of antigens to DC cells, the reference does teach the use of the vehicles to deliver antigens to, and activate the immunogenicity of, immune cells in vitro for later administration. From the teachings of Tomai indicating the utility of DC cells in such methods, it would have been obvious to those in the art that the methods of using yeast vehicles described by Duke would be an functional alternative to the methods of activating DCs described by Tomai. Thus, the combination of the references renders the claims obvious. While the Tomai reference does not indicate that additional immune response modifiers would be required, such is not necessary where the references teach alternative methods of activating the DCs.

Those in the art would have been motivated to use the methods of Duke in view of the teachings of Duke teaching the benefits of using the yeast vehicles described therein. See e.g.,

column 2, lines 30-45. The fact that Tomai teaches an alternative method for the activation of the DCs does not teach away from the use of the Duke method. Because it would have been apparent to those in the art that the method of Duke could be substituted for the method of Tomai with regards to cell activation, and because the teachings of the two references are otherwise complementary, the combined teachings of the reference render the claimed inventions obvious. Because it is not clear how the teachings of the two references fail to render obvious the claimed compositions, the rejection is maintained.

With respect to the Applicant's assertions of unexpected results, the applicant relies on the same teachings as were previously addressed. The argument is not found persuasive in this instance for the same reasons as indicated above.

The rejection is therefore maintained for the reasons above and the reasons of record.

Conclusion

11. No claims are allowed.

12. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Caplan et al., U.S. 2003/0035810. This reference teaches the use of recombinant bacteria and yeast for the delivery of antigens into animals and cells. Abstract. The reference teaches that the microorganisms carrying the antigens, or nucleic acids encoding such, are phagocytosed into APCs, including dendritic cells. Abstract and page 3, paragraph [0022]. The reference does not however teach isolated DCs into which yeast vehicles have been loaded.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 6/13/05
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Continuation of Attachment(s) 6). Other: copy Filing Receipt mailed 3-20-02.